REMARKS

Amendments

In the interest of expediting the prosecution of this Application, Applicants amend Claim 41. Applicants amend Claim 41 in order to further clarify the subject matter claimed. Applicants reserve the right to reintroduce the original claims in one or more continuation type of application.

Claim 41 is amended to recite "said nucleic acid sequence" instead of "said gene". Support for this amendment is found, for example, in the amended paragraph beginning on page 5, line 9.

Applicants respectfully contend that the amendments will place the case in condition for allowance. No new matter is added in any of the above amendments and the Examiner is respectfully requested to enter the amendments and reconsider the application.

Remarks

Claims 32-43 are pending in the present application.

1. 35 U.S.C. 112, first paragraph.

The Examiner rejects Claims 32-40 and 42-43 under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner rejects these claims for the following reason: "With the exception of SEQ ID NO:1 the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides." (page 4, line 11-13). The Examiner also asserts that the structure of variants and alleles are not defined. The Examiner also cites three cases involving § 112, first paragraph issues and DNA sequences: *Fiers v. Revel*, 25 USPQ2d 1601 (Fed. Cir. 1993); *Fiddes v. Baird*, 30 USPQ2d 1481 (Bd. Pat. App. & Inter. 1994); and, *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1481 (Fed. Cir. 1991). The Examiner alleges these cases support rejection of Claims 32-40 and 42-43 for lack of written description. Applicants respectfully disagree with the Examiner's arguments and traverse this rejection.

The specification provides adequate written description of a method of diagnosing colorectal cancer by determining the expression of a nucleic acid sequence at least 95% identical to SEQ ID No:1 in a first sample comprising colorectal cancer cells from a first individual. The specification provides the complete sequence of SEQ ID No:1. SEQ ID No:1 is a 2103 nucleotide long DNA. The specification teaches that "a nucleic acid is a nucleic acid "colorectal cancer nucleic acid" if the overall homology of the nucleic acid sequence to the nucleic acid sequence encoding the amino acid sequences of the figures is . . . as high as about 93 to 95 or 98%." (page 13, lines 27-31).

Applicants respectfully submit that the specification teaches sufficient distinguishing identifying characteristics of the genus of nucleic acids described in Claim 1. The specification teaches nearly the entire sequence of the nucleic acid: it has at least 95% sequence identity with the SEQ ID NO:1 (page 13, lines 27-31). The specification teaches a physical and/or chemical characteristic of the nucleic acid: it is differentially expressed (either up-regulated or down-regulated) in colorectal cancer when compared to normal tissue (page 6, lines 19-24). The specification also teaches a physical characteristic of the nucleic acid encoded by SEQ ID NO:1: it contains a Pleckstrin domain (page 5, lines 13-15). The specification teaches a functional characteristic in that the nucleic acid encoded by SEQ ID NO:1 encodes a colorectal cancer modulating protein (page 3, lines 4-8). Therefore the nucleic acid sequence encoding a CBK8 allele or variant that has at least 95% identical with the nucleic acid that encodes CBK8 as depicted by SEQ ID NO:1, and that this CBK8 allele or variant contains a Pleckstrin domain, is differentially expressed in colorectal cancer tissue and is a colorectal cancer modulating protein.

In fact, the specification provides an example of a sequence that has at least 95% sequence similarity or identity with the SEQ ID NO:1. The specification cites the sequence of accession no. AW136973 (a copy of which is enclosed) as being "substantially complementary" to the sequence of SEQ ID NO:1. Out of a total of 218 nucleotides, the sequence of accession no. AW136973 shares 214 identical nucleotides (98.2%) with SEQ ID NO:1.

The Examiner has stated: "the skilled artisan cannot envision the detailed chemical

structure of the encompassed genus of polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation" (page 5, lines 8-12). However, Applicants respectfully point out that *reduction to practice has occurred*: in that the nucleotide sequence of CBK8 has been sequenced and corresponds to SEQ ID NO:1. The claimed method encompasses determining the expression of a nucleic acid sequence at least 95% identical to SEQ ID NO:1. The nucleic acid sequence, whose expression is to be determined, is limited to a sequence that is 95% or more identical to SEQ ID NO:1.

The present situation is also distinguished from the situation in *Fiers v. Revel* (25 USPQ2d 1601 (Fed. Cir. 1993)). In *Fiers v. Revel*, the written description requirement of a claim directed to "a DNA which codes for a human fibroblast interferon-beta polypeptide" (*Id.* at 1603) was not met in a specification that merely contained a "reference potential method for isolating [the DNA]" (*Id.* at 1606). In *Fiers v. Revel*, the specification in question did *not* provide *any* nucleotide sequence. In the present situation the complete sequence is provided, i.e., SEQ ID NO:1. Corresponding DNA that have at least 95% similarity or identity can be easily determined using routine experimentation by comparison with SEQ ID NO:1.

The present situation is distinguished from the situation in *Fiddes v. Baird* (30 USPQ2d 1481 (Bd. Pat. App. & Inter. 1994)). In *Fiddes v. Baird*, the written description requirement of a claim directed to "[a recombinant] DNA sequence encoding mammalian basic fibroblast growth factor" (*Id.* at 1481) was not met in a specification that merely taught a "theoretical DNA sequence encoding bovine pituitary FGF" (*Id.* at 1606). In *Fiddes v. Baird*, the specification in question did *not* provide any actual nucleotide sequence. In the present situation the complete sequence is provided, i.e., SEQ ID NO:1. In *Fiddes v. Baird*, it was not known how different another non-bovine mammalian FGF nucleotide sequence would be compared to the theoretical nucleotide sequence of bovine FGF. Such a difference could possibly be far less than 95% similarity or identity. In contrast, corresponding DNA that have at least 95% similarity or identity can be easily determined using routine experimentation by comparison with SEQ ID

NO:1.

The present situation is distinguished from the situation in *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* (18 USPQ2d 1481 (Fed. Cir. 1991)). In *Amgen v. Chugai*, the claims in question are directed to all possible DNA sequences that will encode any polypeptide having an amino acid sequence "sufficiently duplicative" of EPO to possess the property of increasing production of red blood cells (*Id.* at 1026). These claims were found invalid for lack of *enablement* in that the disclosure because, while the disclosure might well have justified a generic claim to similar analogs, but not to claim all EPO gene analogs (*Id.* at 1027). It is also important to note that the ruling from the court in *Amgen v. Chugai* was based upon lack of enablement, not upon lack of written description, which the Examiner alleges is the present situation.

In addition, the Applicants respectfully submit that the situation of Claims 32-40 and 42-43 is similar to Example 14 of the Revised Interim Written Description Guidelines Training Materials (pages 53-55). In Example 14, the claim in question is: "A protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A → B." The specification cited in Example 14 exemplifies a protein isolated from the liver that catalyzes the reaction of A → B, and provides the sequence of the isolated protein as set forth in SEQ ID NO: 3. The specification in Example 14 also contemplates but does not exemplify variants of the protein, provides procedures for making variants, and provides an assay for detecting the catalytic activity of the protein. The present situation is similar in that the present situation exemplifies the nucleotide sequence having SEQ ID NO:1 that is characterized by differential expression in colorectal cancer cells and normal colon tissue. The present specification teaches the procedures for making variants (page 23, line 31 to page 24, line 8) and a method for assaying expression of such variants (page 33, lines 13-32; also, page 54-63, Example 1-3). SEQ ID NO:1 is novel and unobvious. There is actual reduction to practice of the single disclosed species. The specification indicates that the genus of nucleotide sequences must be variants of SEQ ID NO:1 does not have substantial variation since all of the variants must

possess the specific differential expression and must have at least 95% identity to the reference sequence, SEQ ID NO:1. The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference molecule and because of the presence of the method which Applicants have taught for identifying all of the at least 95% identical variants of SEQ ID NO:1 which have differential expression. One of skill in the art should conclude that Applicants were in possession of the necessary common attributes possessed by the members of the genus.

Accordingly, for the foregoing reasons, Applicants submit that the specification provides a fully adequate written description of a method of diagnosing colorectal cancer as presently claimed in Claims 32-40 and 42-43. The Examiner is respectfully requested to withdraw this rejection.

The Examiner rejects Claim 41 under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants disagree with the Examiner's rejection, but for the purpose of expediting prosecution of the present application, Applicants amend Claim 41 by replacing "gene" with "nucleic acid sequence".

As amended Claim 41 has adequately written description in the specification, the Examiner is respectfully requested to withdraw this rejection.

The Examiner rejects Claim 41 under 35 U.S.C. § 112, second paragraph as allegedly having insufficient antecedent basis for the limitation "said gene". In light of the amendment described above, whereby Claim 41 is amended so that the term "said gene" is replaced with "said nucleic acid sequence". Therefore, the Examiner is respectfully requested to withdraw this rejection.

The Examiner rejects Claims 32-43 under 35 U.S.C. § 112, first paragraph as allegedly not enabled for a method of diagnosing colorectal cancer comprising detecting the level of expression of a nucleic acid that is at least 95% identical to SEQ ID NO:1 in a first sample comprising colorectal cancer from a first individual and comparing the expression in a second normal colon sample wherein an increase in expansion in the first sample is indicative of colorectal cancer. Applicants respectfully traverse this rejection.

The test for enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *United States v. Teletronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988).

Applicants contend that it is merely a matter of routine experimentation to determine what nucleic acid sequences are at least 95% identical to SEQ ID NO:1. What is merely required is to sequence the nucleic acid in question, and compare this sequence with the sequence of SEQ ID NO:1. In addition, it is a matter of routine experimentation to determine whether such a nucleic acid sequence is differentially expressed in colorectal cancer cells as compared to normal colon tissue. The Examiner asserts that "the specification fails to disclose a nucleic acid molecule 95% identical to SEQ ID NO:1 that can be used to discriminate the individual that has primary or metastatic colorectal cancer from the individual that is disease-free" (page 8, lines 15-18). Applicants respectfully point out that the disclosure of SEQ ID NO:1 itself is the teaching of a nucleic acid sequence that is 100% identical to SEQ ID NO:1.

Further, the Examiner has stated that the specification is "enabling for a method of diagnosing colorectal cancer comprising detecting the level of expression of SEQ ID NO:1 in a first sample comprising colorectal cancer from a first individual and comparing the expression in a second normal colon sample wherein an increase in expansion in the first sample is indicative of colorectal cancer" (page 7, lines 4-8). However, Claim 41 is limited to the nucleic acid sequence being SEQ ID NO:1. Claim 41 is directed to a method that the Examiner has explicitly

stated is enabled by the specification..

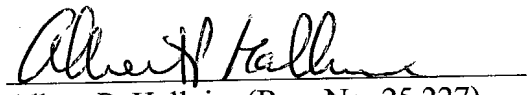
Therefore, as the specification enables Claims 32-43, the Examiner is respectfully requested to withdraw this rejection.

CONCLUSION

In view of the foregoing amendment and remarks, the Applicants believe that the application is in good and proper condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (650) 463-8109.

Respectfully submitted,

Date: December 16, 2003



Albert P. Halluin, (Reg. No. 25,227)
Robin C. Chiang (Reg. No. 46,619)

HOWREY SIMON ARNOLD & WHITE, LLP
301 Ravenswood Avenue
Box 34
Menlo Park, CA 94025
(650) 463-8109